Tasumatrols U−Z, Taxane Diterpene Esters from *Taxus sumatrana*

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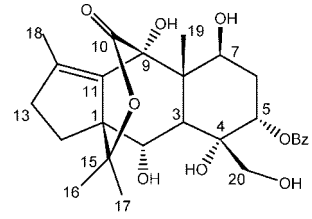
Phytochemical investigation of the leaves and twigs of *Taxus sumatrana* afforded six new taxane diterpene esters, tasumatrols U−Z (**1**−**6**). Compounds **2** and **5** contained a rare five-membered lactone ring at C-8, C-9, C-10, and C-19. The structures were established on the basis of detailed spectroscopic analyses, particularly HRESIMS and 2D NMR techniques. Compound **5** showed cytotoxicity against a human hepatoma (Hep2) cell line.

The discovery of paclitaxel (Taxol) as a potent anticancer drug from *Taxus brevifolia* has motivated many chemists to investigate other species of *Taxus* in order to isolate more effective derivatives and starting materials for semisynthesis.[1−5] Taxol analogues (taxoids) exert their remarkable antitumor activity through inhibition of Ca^{2+}-induced microtubule depolymerization,[6] and some taxoids overcome multidrug-resistant tumors by increasing accumulation of vincristine in cancer cells.[7] To date, more than 500 taxoids have been isolated from different *Taxus* species.[5,8] Taxoids are highly oxygenated and esterified diterpenes, mostly containing a 6/8/6-membered skeleton as in paclitaxel, and have been isolated from different species of yew trees (family Taxaceae). They include taxoids with modified skeletons such as the 11(15→1)-*abeo*-taxanes (5/7/6-membered ring system) and the 2(3→20)-*abeo*-taxanes (6/10/6-membered ring system).[8] We have investigated a taxoid-rich extract of leaves of *Taxus sumatrana* (Miq.) de Laub. (Taxaceae) growing in Taiwan.[9−11] Herein, we report the isolation of six new taxoids, tasumatrols U−Z (**1**−**6**). Tasumatrols U, V, W, Y, and Z (**1**−**3**, **5, 6**) possess an 11(15→1), 11(10→9)-bis-*abeo*-taxane skeleton, while tasumatrol X (**4**) has a 2(3→20)-*abeo*-taxane skeleton. Tasumatrols V (**2**) and Y (**5**) have a rare hydroxy lactone ring between C-10 and C-19.



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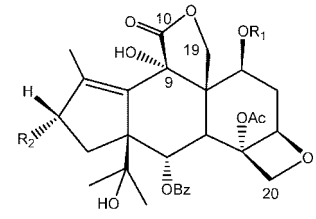
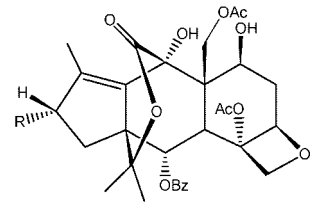
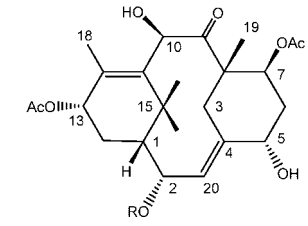


2 R_1 = Ac, R_2 = OH
5 R_1 = H, R_2 = H



3 R = OH
6 R = H



4 R = H
7 R = Ac

Results and Discussion

Solvent fractionation and multiple chromatographic separation over NP- and RP-18 silica gel of an acetone extract of the leaves of *T. sumatrana* afforded six new taxanes, **1**−**6**.

The molecular formula of **1** was established as $C_{27}H_{34}O_9$ by HRESIMS (*m*/*z* 525.2096). The IR spectrum displayed absorption bands diagnostic of hydroxyl (3439 cm^{-1}) and ester (1716 cm^{-1}) functionalities. The ^1H NMR spectroscopic data (Table 1) showed low-field signals of a benzoyl ester at δ_H 8.00, 7.64, and 7.52, together with four methyl singlets of a taxane skeleton at δ_H 2.11, 1.91, 1.33, and 1.14. The ^{13}C NMR data (Table 2) revealed a benzoyl carbonyl signal at δ_C 164.9 in addition to a resonance for a tetrasubstituted double bond (δ_C 131.1, 135.6) that implied the presence of four rings. These data, together with signals for a carbonyl at δ_C 173.2 (C-10), two low-field oxygenated quaternary carbons at δ_C 85.0 (C-9) and 89.4 (C-15), and a quaternary carbon at δ_C 64.2 (C-1), were in good agreement with an 11(15→1), 11(10→9)-bis-*abeo*-taxane skeleton.[12,13] A complete assignment of protons and carbons was assisted by HMQC, COSY, and HMBC experiments (Figure 1). The two methyl protons at δ_H 1.91 (H-16) and 1.33 (H-17) correlated to C-1, while the oxygenated methine at δ_H 4.39 (H-2) correlated to C-1, C-15, C-3 (44.9, d), C-8 (48.0, s), C-14 (24.2, t), and C-15. The two primary alcohol protons at δ_H 3.87 (2H, s, H-20) correlated with the oxyquaternary carbon at δ_C 76.9 (C-4) and the oxymethine at δ_C 71.8 (C-5), proving hydroxylation at C-20. The relative low-field chemical shift of H-5 (δ_H 5.42) implied acylation and was supported by the correlation of H-5 to a benzoyl carbonyl at δ_C 164.9, C-20 (δ_C 63.0), in the HMBC spectrum. The third oxymethine at δ_H 4.30 was assigned to H-7 as a result of its HMBC correlations with C-8 (48.0) and C-9 (δ_C 85.0) and correlation of CH_3-19 to C-3 (δ_C 44.9), C-7 (δ_C 68.3), and C-9. The vinylic methyl at δ_H 2.11 correlated with C-11 (δ_C 131.1) and C-13 (δ_C 39.1). The absence of signals assignable to H-9 and H-10 supported the presence of a six-membered lactone ring involving C-15, C-1, C-11, and C-9, characteristic of wallifoliol analogues.[14,15] COSY experiments showed connectivities between H-2/H-3, H-5/H-6/H-7, and H-13/H-14, verifying the structure proposed for **1** (Figure 1). The large $J_{2,3}$value (11.8 Hz) indicated the opposite configuration of H-2 and H-3. The relative configuration of **1** was proposed on a biogenetic basis and by inspection of the NOESY spectrum, which showed correlations between H_β-19/H-2, H_β-6,H-20; H-20/H-2, H-5, H-19; H-17/H-2, H-16; and H-3/H-7. These data were in accordance with the β-orientation of H-2, H-5, and H-20 and the α-orientation of H-7.

The HRESIMS of **2** revealed a quasimolecular ion peak at *m*/*z*623.2102 $[M + Na]^+$, consistent with the formula $C_{31}H_{36}O_{12}Na$.

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Table 1. ^{1}H NMR Data (500 MHz, $CDCl_3$) of Compounds **1**−**6**[a]

position	1	2	3	4	5	6
1				1.63 m		
2	4.39 d (11.8)	6.21 d (11.3)	6.47 d (11.8)	4.64 d (9.5)	6.17 d (11.2)	6.47 d (12.2)
3	2.54 d (11.8)	2.70 d (11.3)	2.98 d (11.8)	2.55 m 2.00 m	2.59 d (11.2)	2.86 d (12.2)
5	5.42 br s	4.66 d (7.3)	4.83 br d (7.3)	4.49 br s	4.74 d (7.5)	4.77 d (8.5)
6	2.04 m	2.94 m 1.95 m	2.83 m 1.88 dd (15.0,6.5)	2.58 br d (15.3) 1.90 m	2.73 m 1.84 dd (15.0,8.9)	2.83 m 1.88 m
7	4.30 dd (9.5,5.7)	5.43 br t (7.3)	4.42 m	5.08 dd (11.6,5.0)	4.45 br t (9.0)	4.34 dd (9.0,8.5)
10				5.47 s		
13	2.43 m (2H)	4.56 m	4.57 m	5.37 d (9.9)	2.42 m 2.38 m	2.45 m 2.38 m
14	2.30 m 1.55 m	2.19 m (2H)	2.37 dd (14.8,6.7) 2.03 m	2.60 m 2.08 m	2.40 m 1.63 m	2.33 m 1.80 m
16	1.91 s	1.06 s	1.26 s	1.15 s	1.17 s	1.33 s
17	1.33 s	1.25 s	1.35 s	1.20 s	1.20 s	1.36 s
18	2.11 s	2.28 s	2.11 s	1.94 s	2.23 s	2.05 s
19	1.14 s	5.16 d (9.7) 4.96 d (9.7)	5.32 d (13.2) 4.90 d (13.2)	1.37 s	5.00 d (10.0) 4.94 d (10.0)	5.33 d (13.5) 4.88 d (13.5)
20	3.87 br s (2H)	4.82 d (8.7) 4.40 d (8.7)	4.76 d (8.5) 4.30 d (8.5)	5.70 d (9.5)	4.81 d (9.0) 4.34 d (9.0)	4.84 d (8.5) 4.28 d (8.5)
OCOPh						
o-	8.00 d (7.2)	7.98 d (7.2)	7.96 d (7.3)		7.95 d (7.5)	7.96 d (7.1)
m-	7.52 t (7.2)	7.46 t (7.2)	7.47 t (7.3)		7.46 t (7.5)	7.47 t (7.1)
p-	7.64 t (7.2)	7.59 t (7.2)	7.50 t (7.3)		7.57 t (7.5)	7.60 t (7.1)
Ac-4		1.54 s			1.55 s	1.64 s
Ac-5						
Ac-7		2.03 s		2.16 s		
Ac-13				2.01 s		
Ac-19			2.21 s			2.21 s

[a] *J* values (Hz) in parentheses.

The ^{1}H NMR spectrum showed the presence of two acetate (δ_H 1.54, 2.03 and δ_C 20.5, 20.7, 170.1, 170.2) esters and a benzoate (δ_H 7.98, 7.59, 7.46 and δ_C 164.3, 129.9, 128.1, 129.1, 133.0) ester. The oxyquaternary carbon at δ_C 83.5 was assigned to C-15 of an 11(15→1)-*abeo*-taxane skeleton bearing a dimethyl carbinol group at C-1, as indicated by the HMBC correlations of H-16 and H-17 to both C-1 and C-15. The relative upfield shift of the latter when compared to that of **1** (δ_C 89.4) and the shift of the C-10 carbonyl (δ_C 176.1 instead of δ_C 173.2 in **1**) suggested the absence of the six-membered lactone ring. The high-field-shifted methyl singlet assignable to H-19 was absent and was replaced by oxymethylene protons at δ_H 5.16 and 4.96 that correlated to C-7 (δ_C 70.1), C-8 (δ_C 49.3), C-9 (δ_C 78.6), and C-10 (δ_C 176.1, CO), disclosing a rare five-membered lactone ring involving C-19, C-8, C-9, and C-10. A second set of oxymethylene protons resonated at δ_H 4.82 and 4.40 and exhibited HMBC correlations to C-3 (δ_C 40.0), C-4 (δ_C 79.5), and C-5 (δ_C 83.5), indicating a 4,5-oxetane ring. The HMBC correlation of H-2 (δ_H 6.21) to the benzoyl carbonyl (δ_C 164.3), C-1 (δ_C 60.9), and C-15 (δ_C 83.5) was used to locate the benzolyloxy group at C-2, while a correlation of H-7 (δ_H 5.43) to the acetate carbonyl (δ_C 170.2) helped position an acetoxy group at C-7, which was supported by COSY correlations between H-2/H-3 and H-5/H6/H-7. A hydroxy substitution at C-13 was evident from COSY correlations of the oxymethine at δ_H 4.56 with H-14 together with HMBC correlations of H-18 (δ_H 2.28) to C-13 (δ_C 79.5) and C-11 (δ_C 133.1), and of H-14 to C-11 and C-12 (δ_C 148.0). The NOESY correlations between H-19/H-2, H_β-6, H-20; H-2/H-17, H-19, H-20; H-13/H-16, H-18; and H-5/H_α-6 and H_α-3/H-7 were in agreement with the β-orientation of H-2, H-13, H-19, and H-20 as well as the α-orientation of H-5 and H-7 (Figure 2).

Tasumatrol W (**3**) was assigned the molecular formula $C_{31}H_{36}O_{12}$, as deduced from the HRESIMS. The NMR spectroscopic data (Tables 1 and 2) revealed a taxane skeleton similar to that of **1**. The ^{1}H NMR spectrum disclosed a 4,5-oxetane ring (δ_H 4.76, 4.30 correlated to C-3, C-4, and C-5) in addition to an oxygenated functionality at C-19 (δ_H 5.32, 4.90, correlated to C-3, C-8, and C-9). A benzoyl ester was detected at δ_H 7.96, 7.50, 7.47 and was attached to C-2 (correlation of H-2 to benzoyl carbonyl), in addition to two acetate esters that were located at C-4 and C-19, respectively, with the aid of HMBC data. The two exomethine protons at δ_H 4.42 and 4.57 were positioned, in turn, at C-7 and C-13, considering the COSY correlations of H-7/H-6/H-5 and H-13/H-14 and HMBC correlations between H-6/C-7, H-3/C-7, and H-18/C-11, C-13, in addition to the absence of HMBC correlations from either H-7 or H-13 to any carbonyl carbon. The NOESY correlations (Figure 3) between H-17/H-2; H-16/H-13; H-19/H-2, H-20; and H-3/H-5, H-7 were used to determine the β-orientation of H-2, H-20, and H-13 and the α-orientation of H-5 and H-7.

The HRESIMS of **4** exhibited a molecular ion at *m*/*z* 473.2151 $[M + Na]^+$, corresponding to $C_{24}H_{34}O_8Na$. The ^{1}H NMR data revealed four methyl singlets of a taxane skeleton (δ_H1.15, 1.20, 1.37, and 1.94), five oxymethines (δ_H 4.64, 4.49, 5.08, 5.37, and 5.47), along with one olefinic proton (δ_H5.70) and two acetate moieties (δ_H2.01 and 2.16). The ^{13}C NMR spectrum indicated the presence of a ketone (δ_C 213.3), a trisubstituted double olefin (δ_C 129.3, 136.7), a tetrasubstituted olefin (δ_C 134.0, 135.2), and signals

Table 2. ^{13}C NMR Spectroscopic Data (125 MHz, $CDCl_3$) of Compounds **1**−**6**[a]

carbon	**1**[b]	**2**	**3**	**4**	**5**	**6**
1	64.2 s	60.9 s	59.7 s	49.8 d	63.3 s	62.1 s
2	68.4 d	68.5 d	69.1 d	67.4 d	69.5 d	69.6 d
3	44.9 d	40.0 d	43.0 d	35.6 t	41.8 d	43.3 d
4	76.5 s	79.5 s	80.4 s	136.7 s	80.3 s	80.3 s
5	71.8 d	83.5 d	84.7 d	68.4 d	84.5 d	84.6 d
6	32.7 t	33.0 t	37.3 t	35.6 t	35.4 t	37.2 t
7	68.3 d	70.1 d	70.8 d	70.6 d	69.3 d	70.7 d
8	48.0 s	49.3 s	52.5 s	52.7 s	50.4 s	52.1 s
9	85.0 s	78.6 s	81.6 s	213.3 s	80.8 s	82.2 s
10	173.2 s	176.1 s	174.8 s	77.5 d	177.7 s	175.2 s
11	131.1 s	133.1 s	130.7 s	135.2 s	133.2 s	127.2 s
12	135.6 s	148.0 s	140.7 s	134.0 s	146.7 s	139.4 s
13	39.1 t	79.5 d	79.6 d	70.0 d	39.5 t	39.0 t
14	24.2 t	40.8 t	37.6 t	35.1 t	29.2 d	25.7 t
15	89.4 s	83.5 s	90.4 s	37.3 s	77.0 s	91.2 s
16	22.1 q	26.1 q	24.9 q	24.2 q	26.4 q	22.1 q
17	23.7 q	26.6 q	22.6 q	37.3 q	26.3 q	24.3 q
18	13.4 q	14.3 q	11.0 q	18.3 q	17.4 q	14.0 q
19	11.2 q	66.9 t	62.2 t	21.0 q	66.8 t	62.2 t
20	63.0 t	73.9 t	74.0 t	129.3 d	74.4 t	74.0 t
OCOPh	164.9 s	164.3 s	165.3 s		164.6 s	165.3 s
i-	131.2 s	129.9 s	130.0 s		130.6 s	130.1 s
o-	129.4 d	129.1d	129.4 d		129.4 d	129.3 d
m-	128.6 d	128.1 d	128.7 d		128.5 d	128.6 d
p-	133.1 d	133.0 d	133.7 d		133.3 d	133.4 d
Ac-4		170.1 s, 20.5 q	169.9 s, 20.6 q		169.6 s, 20.9 q	169.5 s, 21.2 q
Ac-5						
Ac-7		170.2 s, 20.7 q		170.0 s, 21.0 q		
Ac-13				169.9 s, 21.0 q		
Ac-19			170.4 s, 21.4 q			169.8 s, 20.6 q

[a] Assignments were aided by HMQC and DEPT techniques. [b] Multiplicity, s = C, d = CH, t = CH_2, q = CH_3.

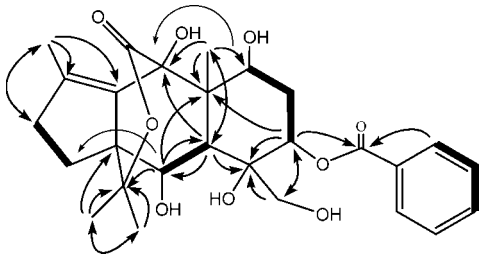

Figure 1. Key HMBC (H⤳C) and COSY (HH) correlations of **1**.

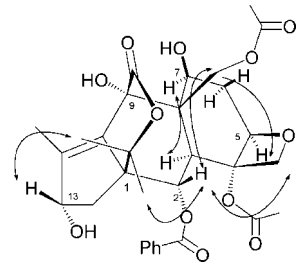

Figure 3. Key NOESY correlations of **3**.

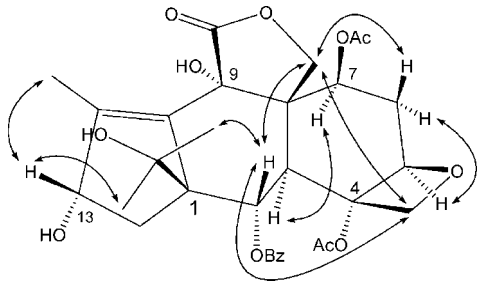

Figure 2. Selected NOESY correlations of **2**.

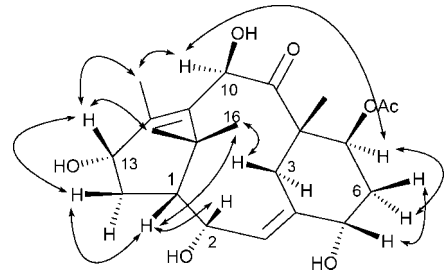

Figure 4. Key NOESY correlations of **4**.

of two acetate moieties (δ_C 170.0, 21.0, 169.9, 21.0), which were supportive of a tricyclic taxane. Both methyl singlets at 1.20 and 1.15 (H-17, H-16) correlated to C-1 (49.8) and C-15 (37.3), whereas the methyl singlet at 1.94 (H-18) correlated to C-11 (135.2) and 134.0 (C-12). The NMR and MS data suggested the presence of a 2(3→20)-*abeo*-taxane having a 6/10/6-membered ring system,[16] which was supported by COSY correlations between H-13/H-14/H-1/H-2/H-20 and H-5/H-6/H-7. The HMBC spectrum revealed correlations between H-3 (δ_H 2.55)/C-4 (δ_C 136.7), C-20 (δ_C 129.3), C-8 (δ_C 52.7), and C-9 (δ_C 213.3), implying a 20(4)-double bond and a carbonyl at C-9. The oxymethine resonating at δ_H5.47 was assigned to H-10 due to its HMBC correlations to C-9, C-11 (δ_C 135.2), and C-15 (δ_C 37.3). One acetyloxy group was attached to C-7 (HMBC correlations to C-8 to acetate carbonyl at δ_C 170.0), while the other acetyloxy was assigned to C-13 (correlations of H-13/C-11, C-14, and H-18/C-12, C-13). The NOESY correlations between H-1/H-2, H-16, H$_\beta$-14; H-5/Hβ-6; and H-13/H$_\beta$-14, H-17 were in agreement with a β-configuration of H-2, H-5, and H-13, while correlations between H-7/H$_\alpha$-6, H-10 favored the α-configuration of H-7 and H-10 (Figure 4). The absence of any NOE effect between H-19 and H-7 was supportive of the α-orientation of H-7.

The HRESIMS data of **5** suggested a molecular formula of $C_{29}H_{34}O_{10}$, and its NMR spectroscopic data indicated a similar taxane skeleton to **2**, with 4,5-oxetane and 10,19-lactone rings (Tables 1 and 2). However, the NMR data indicated the presence

of one benzoyl and one acetate ester only and two oxymethines instead of three in the case of **2**. The oxymethine at δ_H 4.45 showed a HMBC correlation to C-19 (δ_C 66.8) and was assigned to H-7, suggesting a hydroxy substitution at C-7 (δ_C 69.3). In turn, a benzoyloxy group was positioned at C-2 (from a correlation of H-2 to the benzoyl carbonyl). The structure was further confirmed by HMBC correlations between H-2/C-1 (δ_C 63.3), C-3 (δ_C 41.8), C-15 (δ_C 77.0); H-3/C-4, C-7, C-9 (δ_C 80.8); H-20/C-3, C-4, C-5; H-19/C-10 (δ_C 177.7); H-16/C-1, C-15, C-17; and H-18/C-12, C-13 (δ_C 39.5, t). The NOESY correlations of H-2/H-17, H-19, H-20; H-5/H_α-6; and H-3/H-7 favored the β-orientation of H-2, H-19, and H-20 as well as the α-orientation of H-5 and H-7.

The HRESIMS of **6** gave a molecular ion at *m/z* 607.2152 [M + Na]$^+$ indicating a molecular formula of $C_{31}H_{36}O_{11}$, showing this to be a similar compound to **3** but lacking one oxygen atom. The ^{1}H NMR data revealed three methyl singlets at δ_H 1.33 (H-16), 1.36 (H-17), and 2.05 (H-18), an oxetane methylene at δ_H 4.84 and 4.28 (H_2-20), a primary alcohol at δ_H 15.33, 4.88 (H_2-19), and two oxymethines at δ_H 6.47 (H-2) and 4.34, along with two acetate units and one benzoyl moiety. The HMBC data proved the same substitution pattern (one benzoyl at C-2 and two acetates at C-4 and C-19) as in **3**. The methyl protons at δ_H 2.05 (H-18) displayed HMBC correlations to C-11 (δ_C 127.2, s), C-12 (δ_C 139.4, s), and C-13 (δ_C 39.0), verifying the lack of any substitution at C-13. Other HMBC and NOESY correlations were similar to those of **3**.

The 2-*O*-acetate derivative (**7**) of tasumatrol Z (**6**), previously reported from *Taxus x media*,[17] was also isolated during course of fractionation in the present study.

As illustrated in Scheme 1 (Supporting Information), a plausible biogenetic pathway for compounds **5** and **6** has been proposed based on recently isolated diterpenoids. 2-*O*-Deacetyl-13-dehydroxyl-2-*O*-benzoyltaxumairol Q, a derivative of tasumairol Z,[18] might be considered as the precursor. Compounds **5** and **6** are probably transformed from 2-*O*-Deacetyl-13-dehydroxyl-2-*O*-benzoyltaxumairol Q through intermediates **a**, **b**, and **c** via rearrangement, oxidation, hydroxylation, and lactonization. The first step deals with a new bond formation between C-11 and C-9. The final step involves five- or six-membered lactone formation between C-10 and C-19 and between C-10 and C-15, respectively.

Isolation of these taxanes in the course of this experiment affirmed the diversity of taxoid structures that can be elaborated by *T. sumatrana*. The in vitro cytotoxic activities of **1**−**6** were investigated against human Hepa2 (liver carcinoma), WiDr (colon adenocarcinoma), and Hela (cervical epitheloid carcinoma) cell lines, using the MTT assay. Among the compounds tested, compound **5** exhibited cytotoxicity against human Hepa2 tumor cells (ED_{50} 3.5 μg/mL), but was inactive (ED_{50} > 5 μg/mL) against the other two cell lines used. The other compounds were inactive against all of these cell lines.

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a JASCO DIP-1000 polarimeter. IR and UV spectra were measured on Hitachi T-2001 and Hitachi U-3210 spectrophotometers, respectively. The ^{1}H and ^{13}C NMR, COSY, HMQC, HMBC, and NOESY spectra were recorded on a Bruker FT-300 spectrometer or on a Varian Unity INOVA 500 FT-NMR spectrometer at 500 MHz for ^{1}H and 125 MHz for ^{13}C, respectively, using TMS as internal standard. The chemical shifts are given in δ value (ppm) and coupling constants in Hz. HRESIMS spectra were measured on a Bruker Daltonics ApexII mass spectrometer. Silica gel 60 (Merck) was used for column chromatography, and precoated silica gel plates (Merck, Kieselgel 60 F-254, 1 mm) were used for preparative TLC. Sephadex LH-20 was obtained from Amersham Pharmacia Biotech AB, Uppsala, Sweden. LiChrospherSi 60 (5 μm, 250-10, Merck) and LiChrospher100 RP-18e (5 μm, 250-10, Merck) were used for NP-HPLC and RP-HPLC, respectively.

Plant Material. Leaves of *Taxus sumatrana* (Miq.) de Laub. were collected from Kaohsiung County, Taiwan, at an altitude of 1000 m in March 2002. This species was identified by one of the authors (C.-T.C.). A voucher specimen (TPG 8-8) has been kept in the School of Pharmacy, College of Medicine, National Taiwan University, Taipei, Taiwan.

Extraction and Isolation. The dried leaves and twigs (15.5 kg) were ground and extracted three times with acetone at room temperature. The combined extracts were filtered and concentrated under vacuum to obtain a crude extract (3.05 kg). The extract was stirred twice with water (2 × 3.5 L), and the resulting emulsion was separated from the residue and partitioned between EtOAc−water (1:1) to afford an EtOAc extract (173 g). The EtOAc extract was separated on Sephadex LH-20 (MeOH) into two fractions, L_1 and L_2. Fraction L_2 (86 g) was fractionated on a silica gel column using a gradient of *n*-hexane−EtOAc to furnish 18 fractions (L_2-1 to L_2-18). Fraction L_2-4 (1 g) was further separated on Sephadex LH-20 using MeOH to give three fractions (a−c). Part of fraction L_2-4-a (300 mg out of 875 mg) was subjected to RP-HPLC (MeOH−H_2O−CH_3CN, 65:30:5) followed by NP-HPLC (*n*-hexane−CH_2Cl_2−MeOH, 15:5:1) and purification by preparative TLC (silica gel, *n*-hexane−BuOH, 4:1) to yield **6** (4 mg). Fraction L_2-5 (375 mg) was purified on Sephadex LH-20 using MeOH to give three fractions (a−c). Fraction L_2-5b (180 mg) was separated on a flash column using a gradient of *n*-hexane−EtOAc followed by separation on NP-HPLC using *n*-hexane−CH_2Cl_2−MeOH (15:5:1) to give **5** (2 mg). Fraction L_2-8 (1.4 g) was purified on Sephadex LH-20 using MeOH to give three fractions (a−c). Fraction L_2-8a (600 mg) was separated on NP-HPLC using *n*-hexane−CH_2Cl_2−MeOH (15:5:1), followed by separation on RP-HPLC (MeOH−H_2O−CH_3CN, 65:30:5) to give **3** (6 mg) and **2** (5 mg). Fraction L_2-8b (470 mg) was purified on a flash column using a gradient of *n*-hexane−EtOAc followed by separation on RP-HPLC (MeOH−H_2O−CH_3CN, 65:30:5) to give **4** (6 mg). Fraction L_2-9 (1.1 g) was purified on a flash column using a gradient of *n*-hexane−EtOAc followed by separation on RP-HPLC (MeOH−H_2O−CH_3CN, 65:30:5) to yield **1** (11 mg) and **7** (6 mg).

Tasumatrol U (1): colorless powder; $[\alpha]^{26}_D$ −15.2 (*c* 0.2, MeOH); IR (CH_2Cl_2) ν_{max} 3439, 3061, 2926, 1716, 1367, 1263, 1108, 743, 708 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$), see Tables 1 and 2; HRESIMS *m/z* 525.2096 [M + Na]$^+$ (calcd for $C_{27}H_{34}O_9Na$, 525.2100).

Tasumatrol V (2): colorless powder; $[\alpha]^{26}_D$ +69.6 (*c* 0.2, MeOH); IR (CH_2Cl_2) ν_{max} 3419, 2924, 1717, 1274, 1068, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$), see Tables 1 and 2; HRESIMS *m/z* 623.2102 [M + Na]$^+$ (calcd for $C_{31}H_{36}O_{12}Na$, 623.2104).

Tasumatrol W (3): colorless powder; $[\alpha]^{26}_D$ −33.2 (*c* 0.2, MeOH); IR (CH_2Cl_2) ν_{max} 3439, 3061, 2926, 1716, 1603, 1584, 1373, 1276, 1113, 1085, 1049, 737, 714 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$), see Tables 1 and 2; HRESIMS *m/z* 623.2102 [M + Na]$^+$ (calcd for $C_{31}H_{36}O_{12}Na$, 623.2104).

Tasumatrol X (4): colorless powder; $[\alpha]^{26}_D$ −84.0 (*c* 0.2, CH_2Cl_2); IR (CH_2Cl_2) ν_{max} 3445, 2925, 1735, 1372, 1243, 1028, 1000 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$), Tables 1 and 2; HRESIMS *m/z* 473.2151 [M + Na]$^+$ (calcd for $C_{24}H_{34}O_8Na$, 473.2148).

Tasumatrol Y (5): colorless powder; $[\alpha]^{26}_D$ +129.2 (*c* 0.2, CH_2Cl_2); IR (CH_2Cl_2) ν_{max} 3439, 2925, 1716, 1370, 1274, 1115, 1027, 711 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$), see Tables 1 and 2; HRESIMS *m/z* 565.2053 [M + Na]$^+$ (calcd for $C_{29}H_{34}O_{10}Na$, 565.2050).

Tasumatrol Z (6): colorless powder. $[\alpha]^{26}_D$ −69.8 (*c* 0.2, CH_2Cl_2); IR (CH_2Cl_2) ν_{max} 3447, 2925, 2853, 1717, 1280, 1243, 1108 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$), see Tables 1 and 2; HRESIMS *m/z* 607.2152 [M + Na]$^+$ (cald for $C_{31}H_{36}O_{11}Na$, 607.2155).

Cytotoxicity Assay. Cytotoxicity was determined against Hep2 (human liver carcinoma), WiDr (human colon adenocarcinoma), and Hela (human cervical epitheloid carcinoma) tumor cells, using a MTT assay method. The assay procedure was carried out as previously described.[19] ED_{50} values were defined by a comparison with the untreated cells as the concentration of test sample resulting in 50% reduction of absorbance. Camptothecin was used as the positive control and exhibited ED_{50} values of 0.02, 0.07, and 0.19 μg/mL against Hep2, WiDr, and Hela cells, respectively.

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Supporting Information Available: Biogenetic scheme for **5** and **6**. This information is available free of charge via the Internet at http://pubs.acs.org.

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